THE EFFECT OF ELEVATED LEVELS OF MATERNAL CORTICOSTERONE DURING THE NEONATAL PERIOD ON OFFSPRING D2 RECEPTOR FUNCTION

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ABSTRACT

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Long-term behavioral abnormalities have been shown in offspring of mothers who experienced stress during pregnancy. Animal studies looking at perinatal stress have demonstrated offspring behavioral effects such as enhanced anxiety, an increased susceptibility to depression-related behavior, and permanent neuroendocrine changes. Glucocorticoids have been implicated as a possible mediator of long-term prenatal stress effects. Corticosterone (CORT), the principal glucocorticoid in rats, is the end product of the endocrine response to stress via activation of the hypothalamic-pituitary-adrenal axis (HPA). The early postnatal period in the rat, which is the developmental equivalent of the third trimester in humans, is a time of rapid receptor proliferation for key neurotransmitter systems involved in the behavioral effects seen following exposure to stress. The dopaminergic system has been implicated in several psychiatric disorders thought to be affected by perinatal stress; however, very little research has been done to directly examine the effects of elevated CORT during the neonatal period on long-term receptor changes in the dopamine (DA) pathway. This research examined the effects of elevated levels of maternal CORT, during the neonatal period, on the functional sensitivity of D2 receptors in the mesolimbic DA pathway, a region involved in emotion and reward. I found that the effects of neonatal CORT were gender specific. Males, while not showing a change in D2 receptor functional sensitivity, exhibited baseline changes that may be indicative of anhedonia. Females, on the other hand, exhibited an

altered functional sensitivity of D2 receptors, as well as baseline, stress-induced, and D2 receptor-mediated differences in HPA activity. These changes are thought to be in brain pathways that affect emotional responsiveness, and may be significant in the expression of psychopathology. Together, the data demonstrate that elevated levels of maternal CORT during the neonatal period results in gender-specific changes that may predispose offspring to neuropsychiatric disturbances.

Dr. Bethany Neal-Beliveau, Ph.D., Chair

TABLE OF CONTENTS